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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,666	11/15/2001	David Botstein	P2730P1C42	4941

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,666	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *121-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *121-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 14 October 2005 has been entered in full. Claims 119 and 120 are cancelled. Claims 121-131 are under examination. The Goddard Declaration filed on 14 October 2005 under 37 CFR 1.132 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement(s)(IDS) filed 14 October 2005 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

35 USC § 101 and Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 121-131 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The basis for this rejection is set forth at pages 2-5 of the previous Office Action (14 July 2005).

Applicant maintains that a prima facie case has not been made for lack of utility by the Examiner and that the specification provides sufficient disclosure to establish a

specific, substantial and credible utility for the PRO1185 polypeptide SEQ ID NO:401 and other native polypeptides with 90-99% identity to the PRO1185 polypeptide. Applicant argues that the nucleic acid encoding PRO1185 is overexpressed in human tumor tissues as compared to a non-cancerous human tissue control. Applicant submits a Declaration by Dr. Audrey Goddard for support. Dr. Goddard states that a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal samples is useful as a marker for the diagnosis of cancer for monitoring cancer development and/or for measuring the efficacy of cancer therapy. Applicant argues against the references submitted by the Examiner (Pennica *et al.,* Konopa *et al.* and Haynes, all of record). Applicant states that the references do not show that a lack of correlation between DNA amplification and elevated mRNA levels, in general, exists. Applicant discusses references and declarations previously submitted (Orntoft *et al.,* Hyman *et al.,* Pollack *et al.,* Hanna, Mornin and Ashkenazi Declaration, all of record). Applicant maintains that if a gene is amplified in cancer, it is more likely than not that the encoded protein will also be expressed at an elevated level. Applicant maintains that even when the protein is not overexpressed, an assay relying on both tests leads to a more accurate classification of the cancer and a more effective treatment of it. Applicant states that, as evidenced by the Ashkenazi Declaration and the teachings of Hanna and Mornin, one skilled in the art would appreciate that simultaneous testing of gene amplification and gene product overexpression enables more accurate tumor classification, even if the gene-product, the protein, were not overexpressed.

The Examiner has discussed the references and declarations submitted by Applicant in the previous Office Action. The arguments are not deemed persuasive for reasons of record. The Declaration by Dr. Goddard has been fully considered but is not deemed persuasive. The PRO1185 gene has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. The specification merely demonstrates that the PRO1185 nucleic acid was amplified in some cancers. No mutation or translocation of PRO1185 has been associated with any type of cancer versus normal tissue. It is not known whether PRO1185 is expressed in *corresponding* normal tissues, and what the relative levels of expression are. In the absence of any of the above information, all that the specification does is present evidence that the DNA encoding PRO1185 is amplified in a variety of samples, including some normal tissues, and invites the artisan to determine the significance of this increase. One cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. It remains that, as evidenced by references submitted by the Examiner, the issue is simply not predictable, and the specification presents a mere invitation to experiment. Furthermore, the Declaration does not provide data such that the Examiner can independently draw conclusions. Only Dr. Goddard's conclusions are provided in the declaration.

As was stated in the previous Office Action, there is great unpredictability regarding the nature of the instant invention and the state of the art. Increased copy number of DNA does not provide a readily apparent use for the polypeptide, for which

there is no information regarding level of expression, activity or role in cancer. The specification fails to teach that PRO1185 protein levels increase.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claims 121-131 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pages 4-5 of the previous Office Action (14 July 2005).

Applicant incorporates their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicant's arguments have been fully considered but are not found to be persuasive for reasons of record and the reasons discussed above in the maintained 35 USC 101 rejection.

35 USC § 112, First Paragraph, Written Description

Claims 121-123 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification provides adequate written description for SEQ ID NO:401. The instant claims are drawn to *native sequence* polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with SEQ ID NO:401. The term native sequence encompasses naturally-occurring truncated or secreted forms, naturally-occurring variant forms and naturally-occurring allelic variants of the PRO polypeptide. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The basis for this rejection is set forth at pages 5-7 of the previous Office Action (14 July 2005).

Applicant discusses the legal test for written description and various case law. Applicant states that the Examiner directed Applicant's attention to Example 14 of the Synopsis of Application of Written Description Guidelines. Applicant argues that the guidelines state that the protein variants meet the requirement of 35 USC 112, first paragraph, as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if the procedures for making such variants is routine in the art, the specification provides an assay for detecting the functional activity of the protein and the variant proteins possess the specified functional activity and at least 95% sequence identity to the reference sequence. Applicant argues that the instant claims recite a specific functional limitation that the nucleic acid encoding the native sequence polypeptides are overexpressed in lung or colon tumors. Applicant argues that Example 170 in the instant specification, sets forth a gene amplification method and provides step-by-step guidelines and protocols for gene amplification assays for determining whether a gene which encodes

for the native polypeptide having at least 90% identity to PRO1185 is overexpressed in lung or colon tumors. Applicant points to the specification's disclosure of methods for the determination of percent identity, and assays for identification of nucleic acids and for support of the functional limitation in the claims. Applicant urges that the skilled artisan can readily test native polypeptide sequences for identity and whether or not the encoding nucleic acids are amplified in tumors.

Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner cannot find where a suggestion was made to Applicant to examine Example 14 of the Synopsis of Application of Written Description Guidelines was cited, however, the instant claims are not applicable to this example. The instant specification contemplates but does not exemplify variants of the protein wherein the variant can have any number of substitutions, deletions, insertions and/or additions in SEQ ID NO:401, wherein said nucleic acid encoding said polypeptide is overexpressed in lung or colon tumor cells. The specification does not provide any guidance as to what changes should be made and which regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:401 that exist, while still maintaining function. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function. Furthermore, the term native sequence encompasses naturally-occurring truncated or secreted forms, naturally-occurring variant forms and naturally-occurring allelic variants of the PRO polypeptide. None of these sequences meet the written description

provision of 35 USC 112, first paragraph. The specification only shows possession of a single species, not naturally-occurring forms or variants.

The courts have specifically stated that the skilled artisan cannot envision the *detailed chemical structure* of an encompassed polypeptide until the structure is disclosed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In the instant case, SEQ ID NO:401 has been disclosed, but no native sequence variants thereof have been disclosed regardless of whether or not they are encoded by nucleic acids that are amplified in tumors. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factors present in the claims are a partial structure in the form of a recitation of percent identity, a requirement that the

sequence be native, and a requirement that the encoding nucleic acids are amplified in lung and colon tumors. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function. Additionally, there is the issue of whether or not the single disclosed embodiment is actually amplified in lung or colon tumors (see maintained rejections under 35 U.S.C. §§ 101 and 112, first paragraph, above). Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RMD
1/6/06

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER

1/9/06

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